REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated April 29, 2005 are respectfully requested. Applicants petition the Commissioner for a 2-month extension of time. A separate petition accompanies this amendment.

I. Amendments

Claim 7 is amended to clarify the plasma is less than ten percent by volume of the recited gas or vapor.

No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 7 and 31 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

With regard to claim 7, the Examiner objects to the language "less than ten percent." Specifically, the Examiner objects states that while percentages themselves do not have units, it is necessary to know what units were used to calculate the percentage. Claim 7 is amended to clarify that the plasma is formed of a carrier gas and less than ten percent by volume of a gas or vapor selected from oxygen, water, ammonia, ammonium hydroxide, an organic amine, an alcohol, an aldehyde, a carboxylic acid and an ester.

With regard to claim 31, the Examiner objects to the language "homofunctional" as allegedly unclear. Specifically, the Examiner questions what there is to alternate as the functional groups are the same. Applicants respectfully point out that "homofunctional" refers to "molecules" in the claim. Therefore, the functional groups of each molecule is the same, however, the functional groups of alternate molecules may not be the same.

Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph is respectfully requested.

III. Rejection under 35 U.S.C. § 102

Claims 1-2 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Kunz *et al.* (U.S. Patent No. 6,733,847).

These rejections are respectfully traversed.

A. The Present Invention

The present invention describes a method of forming a coating having a selected surface density of a selected chemical group on the surface of a substrate. The method comprises the steps of:

(a) exposing the surface of the substrate to a plasma within a plasma chamber maintained substantially at atmospheric pressure, to form one or more active species on said substrate surface, until a desired surface density of the active species is formed;

(b) in the absence of exposure to plasma, exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group; and

(c) optionally contacting the exposed surface to a surface-modifying group under conditions effective to covalently attach the surface-modifying group to said functional group,

where the selected chemical group on the surface is the stable functional group or the surface-modifying group covalently attached thereto.

B. The Prior Art

Kunz et al. disclose a process for the production of a strongly adherent coating. The process includes subjecting the substrate to a low-temperature plasma discharge (among others). The substrate is precoated with at least one

electron or hydrogen donor compound with at least one ethylenically unsaturated group and reacted with the free radicals formed there. The substrate is then coated with a composition comprising at least one ethylenically unsaturated monomer or oligomer and cured.

C. Analysis

According to M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

The present invention claims a method of forming a coating on the surface of a substrate. The method includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. Kunz *et al.* fail to teach this claimed step.

Kunz *et al.* teach activating a substrate by low-temperature plasma discharge. The substrate is then precoated with an electrode or hydrogen donor compound each containing at least one ethylenically unsaturated group as a coinitiator. Nowhere does Kunz *et al.* disclose stabilizing the active groups formed on the substrate. Nor would one stabilize these groups as they bind to the coinitiator, a necessary feature of Kunz *et al.*

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met and withdrawal of the rejections under 35 U.S.C. § 102(e) is respectfully requested.

IV. Rejections under 35 U.S.C. §103

Claims 1-9, 21-26 and 29-31 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ikada *et al.* (U.S. Patent No. 4,743,258) in view of Yializis *et al.* (U.S. Patent No. 6,118,218) or Krause *et al.* (U.S. Patent No. 5,500,257).

Claims 1-2, 5, 7, 25-26, and 29-31 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gudimenko *et al.* (U.S. Patent App. No. 2003/0021996A1) in view of Yializis *et al.*

Claims 1-9, 21-26 and 29-31 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over O'Brien (U.S. Patent No. 6,709,718) in view of Yializis *et al.* or visa versa.

Claims 7 and 25 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Kunz *et al.*

Claims 1-5, 7-10, 12, 20-24, 26, and 29-30 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Subramaniam (U.S. Patent No. 5,643,580) in view of Yializis *et al.*

Claims 13-15 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Subramaniam (U.S. Patent No. 5,643,580) in view of Yializis *et al.*, and further in view of Valentini or Clapper.

A. The Invention

The present invention is described above.

B. The Prior Art

KUNZ ET AL. is described above.

IKADA ET AL. disclose a blood-compatible material that includes a polymeric base material and water-soluble and substantially nonionic polymers directly attached to the surface of the base material. The polymers may be attached by

forming radicals or peroxides on the surface of the base material and contacting the monomer(s) with the base. The radicals or peroxides may be formed by i.e. low-temperature plasma discharge. Nowhere does Ikada *et al.* show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

YIALIZIS ET AL. disclose an apparatus for producing a glow-discharge plasma at substantially atmospheric pressure comprising a pair of opposing electrodes, at least one of the electrodes comprising a metallic porous layer.

KRAUSE ET AL. describe a method of preparing a fluoropolymer composite tube for use in gas lines. The tube is prepared by activating a formed fluoropolymer substrate by subjecting the substrate to a charged gaseous atmosphere formed by electrically ionizing a gas and subsequently applying a layer of a thermoplastic polymer to the activated fluoropolymer. The ionizing step may be a corona discharge or electrically formed plasma. Nowhere does Krause *et al.* show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group, in the absence of exposure to plasma.

GUDIMENKO ET AL. disclose a process for the production of solid polymeric or composite substrates having surfaces with enhanced release properties. The process includes surface activation of the solid substrate wherein reactive hydrogen groups are formed in the sub-surface region of the substrate. The activated surface is then activated with a silyation solution such that substantially all of the reactive hydrogen groups formed by the activation step are replaced by silicon-containing groups.

O'BRIEN relates to a method for surface treating a porous sheet material. The porous sheet material is contacted with plasma at atmospheric pressure.

SUBRAMANIAM describes biocompatible coatings for medical devices. Plasma is used to functionalize the surface of the medical device with reactive groups. The functionalized surface is then contacted with a bioactive agent or Langmuir-Blodgett film, which is thermochemically covalently coupled to the reactive groups to form the coating.

VALENTINI discloses implantable prosthetic devices having a gold layer on the surface to which bioactive molecules are attached. The device is coated with gold by evaporation, electroplating, sputtering, or electrodeposition. The bioactive molecule is then attached to the gold using "simple chemistry techniques." Molecule coated polymer surfaces (FEP) were also prepared as a control. In this method, surface hydroxyl groups were added to cleaned FEP films by RF glow discharge under pressure. The peptides were rinsed and a peptide was then coupled to the hydroxyl groups. That is, the hydroxyl groups produced by glow discharge form the stable function groups to which the peptides are attached. Nowhere does this reference show or suggest first forming active species on the surface of a substrate, then, in the absence of exposure to plasma, exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

CLAPPER discloses a porous material having a surface chemistry that promotes capillary endothelialization. The material has a porosity that is sufficient to allow capillary endotheliazation. Clapper further discloses binding a cell adhesion molecule to promote ingrowth of endothelial cells into the pores of the material. Nowhere does Clapper show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective, and in the absence of exposure

to plasma, to convert an active species formed during plasma treatment to a stable functional group.

C. Analysis

According to the MPEP § 2143, one of the three basic criteria to establish a *prima facie* case of obviousness is that the prior art references (or references when combined) must teach or suggest all the claim limitations.

1. Rejection over Ikada et al. in view of Yializis et al. or Krause et al.

As noted above, the presently claimed method includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. None of the references show or suggest this claimed step.

As described in Example 2, Ikada *et al.* teach treating a film with a corona discharge and them immersing the corona treated film in an aqueous solution containing a water-soluble and substantially non-ionic polymer. According to the Office action, converting the active species to a stable functional group "may be considered to occur after the corona discharge due to normal exposure to air before the immersion step." However, the active groups are used to react with the polymer and thus cannot be stabilized prior to immersion.

Yializis *et al.* is cited for a teaching of an atmospheric plasma treater to force diffusion of the plasma medium through the porous structure of a porous-metal electrode. Yializis *et al.* fail to teach forming one or more active species on a substrate surface and exposing the surface of a substrate to plasma at atmospheric under conditions to convert the active species to a stable functional group in the absence of exposure to plasma.

Krause *et al.* teach activating a fluoropolymer substrate by subjecting the substrate to a charged gaseous atmosphere. A layer of a thermoplastic polymer is

then applied to the activated fluoropolymer. Nowhere does Krause *et al.* disclose stabilizing the active groups formed on the substrate. Nor would one stabilize these groups as they bind to the thermoplastic layer, a necessary feature of Krause *et al.*

2. Rejection over Gudimenko et al. in view of Yializis et al.

As discussed above, the method of the invention includes a step of exposing the substrate surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma.

Gudimenko *et al.* teach formation of reactive hydrogen groups in a surface region of a solid substrate by corona discharge treatment in air at atmospheric pressure. The reactive groups are then reacted with a silyating agent such that substantially all of the reactive hydrogen groups formed by the activation step are replaced by silicon-containing groups (paragraphs 0027-0030). Thus, the reactive hydrogen groups are replaced by silicon-containing groups and cannot be stabilized prior to contact with the silicon-containing groups. Nor would one be motivated to modify the teaching in Gudimenko *et al.* to stabilize the reactive hydrogen groups as they are necessary for replacement with the silicon-containing groups, a necessary feature of Gudimenko *et al.*

As noted above, Yializis *et al.* also fail to show or suggest converting the active species to a stable functional group.

3. Rejection over O'Brien in view of Yializis et al. or visa versa

As noted above, the presently claimed method includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. Neither of the references show or suggest this claimed step.

O'Brien teaches treatment of a porous film with plasma gas to penetrate into the pores and react with the interior surfaces of the pores to make the film more hydrophilic. O'Brien makes no mention of forming one or more active species on a substrate surface and subsequent exposure to convert the active species to a stable functional group

As noted above, Yializis *et al.* also fail to show or suggest converting the active species to a stable functional group.

4. Rejection over Kunz et al.

The deficiencies in Kunz *et al.* are detailed in section III(C), above. Nor would one be motivated to modify the teaching in Kunz *et al.* to stabilize the ethylenically unsaturated group as they bind to the coinitiator, a necessary feature of Kunz *et al.*

5. Rejection over Subramaniam in view of Yializis et al.

As noted above, the presently claimed method includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. None of the references show or suggest this claimed step.

As described at Col. 2, lines 56-58 and Col. 3, lines 22-24 and 31-33, Subramaniam teaches functionalizing the surface of a medical device by contacting the surface with plasma to form chemically reactive groups. These reactive groups are then contacted with a bioactive agent to covalently bind the agent to the surface by thermochemical reaction with the surface reactive groups. Thus, the reactive groups are used to react with the bioactive agent and cannot be stabilized prior to contact with the agent. Nor would one be motivated to modify the teaching in Subramaniam to stabilize the reactive groups as they are thermochemically reacted with the bioactive agent, a necessary feature of Subramaniam.

Yializis *et al.* is cited for a teaching of an atmospheric plasma treater to force diffusion of the plasma medium through the porous structure of a porous-metal electrode. Yializis *et al.* fail to teach forming one or more active species on a substrate surface and exposing the surface of a substrate to plasma at atmospheric under conditions to convert the active species to a stable functional group in the absence of exposure to plasma.

6. Rejection over Subramaniam in view of Yializis et al., and further in view of Valentini or Clapper

The deficiencies in the combination of Subramaniam and Yializis *et al.* are discussed above.

The Valentini and Clapper references are cited merely for a teaching of the cell-adhesion molecule disclosed in claims 13 and 15. Neither Valentini nor Clapper make up for the shortcoming in the combination of Subramaniam in view of Yializis *et al.*, as discussed above, as neither reference makes any mention of exposing the substrate surface to a selected gas or liquid to convert the active species to a stable functional group.

As shown above, none of the references, alone or in combination, show or suggest exposing the substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

V. Obvious-Type Double Patenting Rejections

Claims 1-10, 12, 21-23, 26, and 29-31 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-8 and 11-17 of U.S. Patent No. 6,159,531 in view of Yializis *et al.*, and further in view of Ikada *et al.*.

Claims 13-15 and 20 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-8 and 11-17 of U.S. Patent No. 6,159,531 in view of Yializis *et al.*, in view of Ikada *et al.*, and further in view of Valentini or Clapper.

Applicants respectfully traverse these rejections.

A. The Present Invention

As noted above, the present invention includes the steps of:

(a) exposing the surface of the substrate to a plasma within a plasma chamber maintained substantially at atmospheric pressure, to form one or more active species on said substrate surface, until a desired surface density of the active species is formed;

(b) in the absence of exposure to plasma, exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group; and

(c) optionally contacting the exposed surface to a surface-modifying group under conditions effective to covalently attach the surface-modifying group to said functional group,

where the selected chemical group on the surface is the stable functional group or the surface-modifying group covalently attached thereto.

B. The 6,159,531 Patent

The claims in Patent No. 6,159,531 relate to a method of treating a medical device briefly comprising:

plasma cleaning the device surface exposed to tissue and/or blood;

functionalizing the surface to provide a plasma-deposited layer having functional groups; and

subjecting the plasma-deposited layer to multifunctional linkers/spacers to form covalent bonds between the linkers/spacers and the functional groups.

C. Analysis

The method of the present invention includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group in the absence of exposure to plasma.

While the method of the '531 patent provides a plasma-deposited layer having functional groups and subjects the layer to multifunctional linkers/spacers to form covalent bonds between the linkers/spacers and the functional groups (optional in the present invention), the '531 patent makes no mention of an intermediate step of converting the active species to a stable functional group, much less converting the active species in the absence of exposure of plasma.

Nor do the cited Beumer *et al.*, Maruyama *et al.*, Li *et al.*, Ikada *et al.* ('258), Krause *et al.*, or Ikada *et al.* ('913) references make up for this lack of teaching for the reasons given above in section III.

In view of the above, Applicants submit that the invention as presently claimed is patentably distinct from U.S. Patent No. 6,159,531. Accordingly, Applicants respectfully request withdrawal of the rejection under the judicially created doctrine of obviousness-type double patenting.

VI. Conclusion

In view of the foregoing, Applicants submit that the claims pending are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,

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